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Canadian Association of Radiologists Journal 62 (2011) 209–214

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Thoracic and Cardiac Imaging / Imagerie cardiaque et imagerie thoracique

Breast Cancer Close to the Nipple: Does This Increase the Risk of Nodal Metastasis at Diagnosis?

Erin I. Lewis, BA[a], Al Ozonoff, PhD[b], Cheri P. Nguyen, MD[c], Michael Kim, BS[a], Priscilla J. Slanetz, MD, MPH, FACR[d,*]

[a]*Department of Radiology, Boston University Medical Center and Boston University School of Medicine, Boston, Massachusetts, USA*
[b]*Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts, USA*
[c]*Department of Radiology, Baystate Medical Center, Springfield, Massachusetts, USA*
[d]*Division of Breast Imaging, Department of Radiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, USA*

Abstract

Background: Previous studies of patients with invasive breast cancer examined, with mixed results, tumour location as a predictor of axillary lymph node metastasis. This study assessed whether tumour location in relation to the nipple impacts the presence of axillary lymph node metastasis at the time of diagnosis.
Methods: A retrospective review was undertaken of the medical records and available imaging of 285 patients diagnosed with invasive breast cancer between January 2001 to June 2007 at Boston University Medical Center. The incidence of axillary lymph node metastasis was correlated with tumour location in relation to the posterior nipple line to control for variation in breast size. Bivariate analysis identified significant variables that were applied to a multiple logistic regression model.
Results: Axillary lymph node metastasis was not significantly associated with tumour proximity to the nipple. In the multivariate logistic regression analysis, known prognostic factors for axillary metastasis, such as surgical size, lymphovascular invasion, and age of diagnosis, were significant, whereas breast density, palpability, and histologic grade were no longer significant.
Conclusions: Our study found that there was no evidence that correlates intramammary tumour proximity to the nipple with the presence of axillary lymph node metastasis at diagnosis. However, known prognostic factors, such as lymphovascular invasion, surgical size, and younger age at diagnosis, are strong independent predictors for axillary lymph node involvement.

Résumé

Contexte: Des études antérieures, dont les résultats sont mitigés, ont été effectuées sur des patientes atteintes d'un cancer du sein invasif et portaient précisément sur l'emplacement de la tumeur en tant que prédicteur d'une métastase ganglionnaire axillaire. L'étude actuelle visait à évaluer si la proximité de la tumeur par rapport au mamelon pouvait influencer la présence de métastase ganglionnaire axillaire au moment du diagnostique.
Méthode: une étude rétrospective a été effectuée et portait sur les dossiers médicaux et les examens d'imagerie disponibles de 285 patientes atteintes d'un cancer du sein invasif de janvier 2001 à juin 2007 au « Boston University Medical Center ». L'incidence de métastase ganglionnaire axillaire a été mise en relation avec la localisation de la tumeur, selon la ligne mamelonaire postérieure, pour tenir compte de la taille du sein. Une analyse bivariée a identifié des variables significatives qui on été appliquées à un modèle de régression logistique multiple.
Résultats: Les métastases ganglionnaires axillaires n'étaient pas significativement associées à la proximité de la tumeur par rapport au mamelon. A l'analyse, les facteurs pronostiques connus pour les métastases axillaires, comme le taille à la chirurgie, l'envahissement lymphovasculaire, et l'âge au diagnostique étaient importants alors que la densité du sein, le grade histologique et la fait que la lésion soit palpable ne l'était plus.
Conclusion: Notre étude montre qu'il n'y a pas d'évidence de relation entre la proximité au mamelon d'une tumeur inta-mammaire et la présence de métastases ganglionnaires axillaires au moment du diagnostique. Toutefois, les facteurs pronostiques connus, comme l'envahissement

* Address for correspondence: Priscilla J. Slanetz, MD, MPH, FACR, Department of Radiology, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, Massachusetts 02215, USA.

E-mail address: pslanetz@bidmc.harvard.edu (P. J. Slanetz).

doi:10.1016/j.carj.2010.03.007

lymphovasculaire, la taille à la chirurgie, et le jeune âge sont des prédicteurs indépendants et forts pour l'atteinte ganglionnaire axillaire.

Key Words: Breast cancer; Axillary lymph node metastasis; Nipple; Mammography

Axillary lymph node metastasis is the single most important parameter in determining breast cancer staging and treatment [1]. Specifically in women with small invasive breast carcinomas (less than 1 cm in size), the detection of axillary lymph node metastasis guides treatment regimens [2]. In the last decade, numerous studies correlated certain breast tumour characteristics, such as tumour size, histologic grade, palpability, and lymphovascular invasion, with a greater chance of axillary metastasis at the time of diagnosis [3–8]. In addition, many researchers have tried to determine if intramammary location of the breast tumour correlates to a higher rate of axillary metastasis and, therefore, a worse prognosis. Although some studies examined the breast 2-dimensionally by comparing medial with lateral locations, other studies tried to look at the breast 3-dimensionally comparing anterior with posterior regions [9–12]. In this retrospective analysis, we assessed tumour location by combining the 2-dimensional and 3-dimensional views of the breast by analysing tumour location on imaging relative to its relationship to the nipple. Because deep lymphatic channels of the breast anastomose at the subareolar plexus, which then drain to the axilla, we proposed that tumours close to the nipple should have a higher rate of axillary lymph node metastasis at diagnosis [13].

Methods

This study was approved by the institutional review board at Boston University Medical Center. Between January 2001 and June 2007, 604 women diagnosed with invasive breast cancer were identified through a computerized database from the Clinical Data Warehouse at Boston University Medical Center. The database provided personal identifying information, medical record number, demographic details, and tumour stage. The information about clinical presentation and course, family history of breast cancer in first-degree relatives, diagnosis, histopathology, and radiologic studies was available from hospital records.

Of the population of 604 with the qualifying diagnosis of invasive cancer, 285 participants (47%) were eligible for the study. Eligibility criteria included any female of any age or ethnicity, histologically confirmed invasive breast cancer stage T1 or higher, available surgical axillary staging data from either sentinel lymph node biopsy or full axillary dissection, available mammogram before cancer treatment, and axillary staging before chemotherapy or radiation therapy. In addition, eligibility required there to be a single breast primary. A total of 319 patients (53%) were excluded from the study for the following reasons: radiologic examinations unavailable (165), axillary status unavailable (97), chemotherapy before axillary staging (30), multifocal cancer (10), no surgery performed (7), unavailable medical records (7), Paget disease (2), and radiation before axillary staging (1).

The mammographic studies were performed by using dedicated equipment (General Electric DMR, Milwaukee, WI; LoRad MIV, Hologic, Bedford, MA; Hologic Selenia, Bedford, MA). By using the cranial-caudal view of the breast, the location of the tumour was demarcated by a board-certified radiologist who specializes in breast imaging with film-screen or digital hard copy images. The distance of the lesion from the nipple was measured in its relation to the posterior nipple line (from the surface of the nipple to the edge of the pectoralis muscle). Two relationships to the posterior nipple line were calculated by using a triangle drawn on the breast. One relationship was calculated of where the lesion fell parallel to the posterior nipple line, and the other relationship was where the tumour fell radially oriented to the posterior nipple line (Figure 1). These measurements allowed standardization, given the differences in breast size among patients. On available ultrasound images, a measurement was taken from the skin surface to the most superficial aspect of the tumour to determine the distance from the skin. The ultrasound studies were performed by using 2 different systems (ATL HDI or iU22 units; Philips, Amsterdam, The Netherlands), with either a 12.5 MHz or 17 MHz linear probe.

Clinical data from the eligible 285 patients with stage T1 or higher breast cancer were collected retrospectively from patient records. The clinical factors assessed were the following: age at diagnosis, history of use of oral contraceptives or hormone replacement therapy, palpability of primary tumour, family history of breast cancer, prior history of breast cancer, or a benign neoplasm. The radiologic factors assessed were the following: density of the breast (classified by using the 4 Breast Imaging Reporting and Data System [BI-RADS] density categories) [14], and the distance from skin on ultrasound. Data about location of tumour were grouped into (1) breast quadrants (upper outer quadrant [UOQ], upper inner quadrant [UIQ], lower outer quadrant [LOQ], lower inner quadrant [LIQ]), periareolar (defined as nipple and $\leq$1 cm from nipple); (2) breast regions (lateral, medial, periareolar); and (3) relationship of tumour to the posterior nipple line (Figures 1 and 2). The pathologic factors evaluated were the following: tumour size (maximum diameter of invasive component measured microscopically), histologic type (based on the International Classification of Diseases, Oncology Classification System), histologic grade (by using the modified Scarff-Bloom-Richardson system), lymphovascular invasion, tumour calcifications present, estrogen/progesterone/Her2 immunohistochemical value, and the number of positive axillary lymph nodes.